Toxicologic Teasers: Testing Your Knowledge of Clinical Toxicology

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The following questions and cases are intended to challenge the physician's knowledge of clinical toxicology. Some of the multiple-choice type of questions listed below may have more than one correct answer.

1. Tachycardia, hypertension, mydriasis, agitation and warm/dry skin are suggestive of which toxidrome?
   a) Anticholinergics
   b) Sympathomimetics
   c) Cholinergics
   d) Sedative-hypnotics
   e) Opiods

2. Acetaminophen ingestions are probably one of the more common accidental ingestions in children.
   a) Based on the history of the ingestion, at what amount (mg/kg) would you be concerned about the possibility of hepatotoxicity?
   b) What serum acetaminophen level would be considered potentially hepatotoxic at 4 hours postingestion?
   c) If N-acetylcysteine (Mucomyst) is required to prevent hepatotoxicity, what is the loading dose (mg/kg) of Mucomyst?

3. List at least 5 poisonings which classically produce an increased anion gap metabolic acidosis.

4. Which of the following medications is/are capable of producing bradycardia after an acute overdose?
   a) Carbamates
   b) Digoxin
   c) Organophosphates
   d) Phenylpropanolamine
   e) Clonidine
   f) Phenylephrine

5. For each of the following poisonings, list the appropriate antidote:
   a) Acetaminophen
   b) Salicylates
   c) Organophosphates
   d) Cyanide
   e) Carbon monoxide
   f) Methemoglobinemia
   g) Benzodiazepines
   h) Morphine
   i) Isoniazid
   j) Ethylene glycol
   k) Iron
   l) Methanol
   m) Phenothiazine (dystonic reactions)
   n) Antihistamines (with very severe anticholinergic symptoms)

6. A 3-year-old child accidentally drank some mouthwash that contained ethanol. He presents in an intoxicated state to the emergency department. Based on the laboratory values listed below, what would you predict this child's blood ethanol level (mg/dL) to be? (Hint; use 4.6 as the conversion factor for ethanol).

   Na = 139 K = 3.5 Cl=103 CO2 = 14 BUN = 13 Creatinine = 0.7 Glucose = 115 Measured serum osmolality = 310

7. List which toxidrome you would expect for each of the acute ingestions listed below.
   a) An over-the-counter cough medication containing diphenhydramine
   b) Cocaine
   c) An insecticide containing carbamates
   d) A mouthwash containing ethanol
   e) A decongestant containing phenylpropanolamine
   f) An analgesic containing codeine

8. A previously healthy 4-year-old child presents with an acute onset of bronchospasm, muscle weakness, vomiting, bradycardia, urinary incontinence, salivation and confusion. What toxidromal class is most likely responsible for these signs and symptoms?
   a) Anticholinergics
   b) Sympathomimetics
   c) Opiods

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d) Cholinergics
e) Sedative-hypnotics

9. Which of the following drug overdoses is/are capable of producing hyperthermia?
   a) Benadryl
   b) Methanol
   c) Cocaine
   d) Amphetamines
   e) Phenobarbital

10. Which of the following agents is/are capable of producing hypotension (and describe the pharmacologic mechanism by which that agent produces hypotension)?
    a) Verapamil
    b) Propanolol
    c) Metamphetamine
    d) Ferrous sulfate
    e) Tricyclic antidepressants

Answers to "Toxicologic Teasers"

1. Although tachycardia, hypertension, mydriasis, agitation and warm skin may be seen with both the anticholinergic and sympathomimetic toxidromes, the finding of dry, warm skin is suggestive of the anticholinergic toxidrome. An example of an anticholinergic ingestion which is not all that uncommon in pediatrics is a diphenhydramine (ie; Benadryl) overdose. In medical school many of us were taught that anticholinergics produce the state of being "mad as a hatter, red as a beet, blind as a bat and dry as a bone." Sympathomimemtics (ie; cocaine, theophylline) usually cause sweating and therefore these patients tend to present with warm, moist skin rather than dry skin.

2. The answers to the three questions regarding acetaminophen poisoning can be remembered by "Dr. Al's 140-140-140 rule" of 140 mg/kg...140 mcg/ml...140 mg/kg.
   a) Based on the history of the ingestion, there is a risk of hepatotoxicity if the ingested amount of acetaminophen was greater than 140 mg/kg.
   b) There is a risk of potential hepatotoxicity if the serum acetaminophen level at 4 hours post-ingestion is greater than 140 mcg/ml.
   c) If N-acetylcysteine is required to prevent hepatotoxicity, the loading dose of Mucomyst is 140 mg/kg.

3. Conditions which classically cause an increased anion gap metabolic acidosis can be remembered by the mnemonic of "M-U-D-P-I-L-E-S:"
   M = Methanol
   U = Uremia
   D = DKA
   P = Paraldehyde
   I = Iron, INH, ibuprophen
   L = Lactic acidosis (ie; carbon monoxide, cyanide)
   E = Ethanol and ethylene glycol
   S = Salicylates

4. ALL of the medications listed are capable of producing bradycardia. Carbamates and organophosphates both produce cholinergic signs and symptoms (which include bradycardia). Digoxin can produce bradycardia by slowing conduction through the AV node. Phenylpropanolamine and phenylephrine are alpha-agonists that are commonly used as decongestants. In an acute overdose situation, both of these alpha-agonists produce hypertension which is accompanied by a reflex (protective) bradycardia. Clonidine-induced bradycardia is due to a generalized sympathetic depression (which also produces hypotension, bradypnea and a depressed mental status).

5. a) Acetaminophen; N-acetylcysteine (Mucomyst)
   b) Salicylates; urinary alkalinization
   c) Organophosphates; atropine +/- pralidoxime (2-PAM; reactivates the cholinesterase enzyme)
   d) Cyanide; Lilly brand cyanide antidote kit (which contains the following three items; amyl nitrate, sodium nitrite & sodium thiosulfate)
   e) Carbon monoxide; oxygen (via non-rebreather mask, endotracheal tube or hyperbaric chamber)
   f) Methemoglobinemia; methylene blue
   g) Benzodiazepines; flumazenil (Romazicon)
   h) Morphine; naloxone (Narcan)
   i) Isoniazid; pyridoxine (vitamin B6)
   j) Ethylene glycol; ethanol drip (although there have been recent reports of using a newer agent [4-methylpyrazole; Fomepizole] to inhibit the alcohol dehydrogenase enzyme)
   k) Iron; desferoxamine (Desferal)
   l) Methanol; ethanol drip (although there have been recent reports of using a newer agent [4-methylpyrazole; Fomepizole] to inhibit the alcohol dehydrogenase enzyme)
   m) Phenothiazine (dystonic reactions); diphenhydramine (Benadryl)
   n) Antihistamines (with very severe anticholinergic symptoms); physostigmine (a reversible inhibitor of the acetylcholinesterase enzyme, which should be used with extreme caution since this antidote may actually precipitate a cholinergic toxidrome)

6. First of all we need to calculate this child's predicted/calculated serum osmolality, which is determined by using the formula:

$$[2 \times Na] + [BUN / 2.8] + [Glucose / 18]$$

Therefore based on the laboratory values provided in this case, the child's calculated serumosmolality would be:

$$[2 \times 139] + [13 / 2.8] + [115 / 18] = 289 \text{ mosm/L}$$

Notice that this formula for determining the calculated serum osmolality does not take into account any other substances that could contribute to the patient's serum osmolality other than sodium, BUN and glucose. Normally the calculated serum osmolality and the actual measured serum osmolality are fairly close if there are no other substances in the patient's blood that could increase the patient's measured serum osmolality. The serum osmolar gap can be determined by the formula:

[measured osmolality] - [calculated osmolality]

The osmolar gap is normally < 5-10 mosm/L. Because of the ethanol that is present in this child's blood the actual serum osmolality that was measured by the laboratory was 310 mosm/L. Based on this formula, this child's osmolar gap would therefore be:

$$[310] - [289] = 21 \text{ mosm/L}$$

And finally, the formula that can be used to estimate this child blood ethanol level based on the osmolar gap is:

$$[4.6] \times [\text{osmolar gap}] = [4.6] \times [21] = 96.6 \text{ mg/dL}$$

Remember that a blood ethanol level > 80 mg/dL is considered legally drunk in the State of Hawaii.

7. a) Anticholinergic
   b) Sympathomimetic
   c) Cholinergic
   d) Sedative-hypnotic
   e) Sympathomimetic
   f) Opiod

8. D (cholinergics). The cholinergic toxidrome can be remembered by the mnemonic "D-U-M-B-L-E-S;"
   D = defication
   U = urinary incontinence
   M = miosis
   B = bronchospasm, bronchorrhea and bradycardia
   L = lacrimation
   E = emesis
   S = salivation

9. A, C and D. Both anticholinergics (ie; Benadryl) and sympathomimetics (ie; cocaine and amphetamines) are capable of producing hyperthermia. Methanol and phenobarbital produce hypothermia rather than hyperthermia.

Medical School Hotline

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licensed in Hawaii, over 1,400 are clinical (non-compensated) faculty and teach medical students, residents, or fellows. Since its founding in 1967, the School has been community-based, integrated into community hospitals and clinics. Today, more than one-third of Hawaii's physicians are alumni. They have made a difference in the quality of medical care in Hawaii.

Despite the current tough economic times and a series of budget cuts that have affected the University, the School of Medicine continues on its mission in keeping the doors open to students from Hawaii and improving the delivery of health care in the State. The faculty also help the State's economy and intellectual climate by generating research and training grants whereby each dollar of the State funds allocated to the School generates three in outside funding. Despite its small size, the School has achieved national and international recognition in its Problem Based Curriculum.

The need to preserve the School's core in these tough times makes it challenging to explore new areas for significant growth or emphasis. That is where friends, old and new, can help. If there is something you think the school should be doing, join and help us. If there is something of importance to you or to your patients, tell us. These suggestions may provide potential possibilities upon which to continue building a world class medical school.

Wanda Jane Kaspari was not a fabulously wealthy woman. Over the years, she and her beloved John accumulated enough assets to enjoy a comfortable retirement. However, Jane Kaspari was a thinker and a planner. She carefully considered how to use her resources to make a permanent difference in her community. Her gift to assist students at the John A. Burns School of Medicine is really an investment in excellent medical care for the people of Hawaii.

10. A, B, D and E are all capable of producing hypotension. Both propanolol and tricyclic antidepressants are capable of producing hypotension by depressing myocardial contractility via their quinidine-like effects. Verapamil can produce hypotension via two pharmacologic mechanisms. One method is via it's vasodilatory effect, and the other is via it's negative inotropic effect on myocardial contractility. Ferrous sulfate can produce hypotension via multiple mechanisms which include;
    a) Hemorrhagic shock (secondary to the direct corrosive effect of iron on the GI tract mucosa that produces GI bleeding),
    b) Distributive shock (due to vasodilatation and capillary leak) and
    c) Cardiogenic shock (due to iron's direct negative cardiac inotropic effect on myocardial contractility).